REMARKS

FORMAL MATTERS:

Claims 1-5, 8, 10-28 and 30-45 are pending after entry of the amendments set forth herein.

Claims 6, 7 and 9 are canceled without prejudice.

Claims 1, 8, 12-16, 28, 30, 34 and 45 are amended. Support for these amendments is found throughout the specification and in the claims as originally filed (see, e.g., original claim 6).

REJECTIONS UNDER §112, ¶2

Claims 1-28, 30-33 and 45 were rejected as being indefinite. This rejection is traversed as applied or as it may be applied to the claims as now pending. Each of these rejections is addressed below.

Claim 1 - "a perfectly matched region of complementarity"

Claim 1 was rejected for recitation of "a perfectly matched region of complementarity". This rejection is avoided by amendment of claim 1.

Claim 8 - "modified DNA"

Claim 8 was rejected for recitation of "modified DNA (mDNA)". This rejection is avoided by amendment of claim 8 to recite exemplary mDNAs.

Claims 15-16 - "distinct sequence"

Claims 15-16 were rejected for recitation of "distinct sequence". This rejection is avoided by amendment of these claims.

Claim 28 - "detectably labeled"

Claim 28 was rejected for recitation of "detectably labeled'. This rejection is avoided by amendment of claim 28.

Claim 30- "no more than about 60°C"

Claim 30 was rejected for recitation of "no more than about 60°C". This rejection is avoided by amendment of claim 30

Applicants respectfully request withdrawal of all rejections of the claims under §112, ¶2.

REJECTIONS UNDER §102(B)

Claim 45 was rejected as being anticipated by Nedbal et al. (Biochemistry 36:13552 (1997)). This rejection is respectfully traversed as applied and as it may be applied to the claim as now pending.

Claim 45 is directed to a method for increasing association of a single-stranded RNA molecule and a single-stranded DNA molecule.

Nebal et al. only describes association of complementary RNA-RNA molecules. Nedbal et al. does not disclose or suggest methods involving association of DNA and RNA molecules.

Withdrawal of this rejection is respectfully requested.

REJECTIONS UNDER §103(A)

Claims 1-28 and 30-33 were rejected as being unpatentable over Cronin et al. (US 6,027,880) in view of Nedbal et al. This rejection is respectfully traversed as applied and as it may be applied to the claim as now pending. This rejection is moot as applied to now-cancelled claims 6-7 and 9.

As set out in MPEP § 2142, each of three basic criteria are required to establish a prima facie case of obviousness: 1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; 2) there must be a reasonable expectation of success; and 3) the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Pending claims 1-5, 8, 10-28 and 30-33 are directed to methods involving forming nucleic acid duplexes between a molecule of RNA and a molecule of DNA.

Cronin et al. only discloses association of DNA-DNA duplexes, and does not teach or suggest nucleic acid duplexes of RNA and DNA.

Nedbal et al. does not cure this deficiency, as this reference only discloses association of complementary RNA:RNA molecules.

Therefore, in view of the above, the prima facie case of obviousness can not be maintained for at least the failure of the combined references to provide one of the basic required criterion, i.e., the cited art does not teach or suggest all the claim limitations.

Furthermore, applicants note that invention as now claimed is associated with surprising results. As set out in the specification at page 6, line 22 to page 7, line 4, and the claimed invention is based on the discovery that performing hybridization in the presence of a specific association enhancer not only accelerates the rate at of duplex formation, but ***also*** greatly increases the specificity or selectivity of

formation of completely matched duplexes over mismatched ones. Moreover, this increase in selectivity is observed for RNA:DNA and DNA:RNA duplexes, but not for formation of DNA:DNA duplexes. The inventors also observed that hybridization in the presence of a specific association enhancer reduces both the GC content sensitivity and temperature sensitivity of the specific hybridization of RNA to DNA, which permits a wider range of probes and/or targets to be used under a common set of hybridization conditions.

A discussion of the results of the inventors' study is set out in the specification at page 28, line 17 to page 30, line 12. For example, the inventors have shown that under standard non-accelerated conditions, DNA:DNA duplexes with single nucleotide mismatch form equally well as those that are fully complementary. Formation of DNA:DNA duplexes was accelerated more than 300-fold in the presence of a specific association enhancer, but had no observable effect on discrimination between the completely matched DNA:DNA duplex and the duplex with a single nucleotide mismatch at any position along the oligo (Example 1, Table 1). Using the same complementary pair of oligos under standard, non-accelerated conditions, but with RNA and DNA, improves the selectivity of formation of matched RNA:DNA duplexes over duplexes with a single nucleotide mismatch (Example 1, Table 1). Surprisingly, addition of an acceleration enhancer also increased discrimination of RNA:DNA duplex formation against single nucleotide mismatched duplexes at all positions, as compared to standard non-accelerated conditions (Experiment 1, Table 1). Using a second, enzymatic assay for duplex detection shows that the association of DNA and RNA molecule has up to 50-fold specificity in the presence of a specific association enhancer (Experiment 2, Table 2).

A variety of methods have previously been shown to accelerate formation of nucleic acid duplex associations; however, to applicants' best knowledge, none has shown a concomitant increase in specificity of association. Moreover, the present inventors have discovered that in the presence of specific association enhancers, mismatched duplexes between RNA and DNA form less favorably at incubation temperatures that are significantly below their Tm, an effect not predicted by, or predictable from, prior observations or theories.

In view of the above, withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number STAN-202.

Respectfully submitted,
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